

What is claimed is:

1. An apparatus for the performing multiplexed patch clamping comprising:
an insulating layer having a plurality of orifices therethrough;
at least one electrode electrically connected with each orifice; and

5 a substrate supporting said insulating layer and said electrodes, wherein said insulating layer, said electrodes, and said substrate are transparent.

2. The apparatus of claim, 1 wherein each of said plurality of orifices has a diameter of about 0.5-5 μm .

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3. The apparatus of claim 1, wherein said electrodes is a ITO electrode.

4. The apparatus of claim 1, wherein each electrode is electrically isolated from the other electrodes.

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5. The apparatus of claim 1, wherein a part of each of said electrode is electrically connected to an orifice.

6. The apparatus of claim 1, wherein each orifice is electrically connected to two

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7. The apparatus of claim 6, wherein one of the two electrodes is a sensing electrode and the other electrode is used to deliver an electrical signal to the orifice.

8. The apparatus of claim 1, wherein an area adjacent to each orifice is coated with a substance to promote cell growth and/or adhesion.

5 9. The apparatus of claim 8, wherein the substance to promote cell growth and/or adhesion is silica (SiO_2), polylysine, and/or collagen.

10. The apparatus of claim 1, further containing a reference electrode.

10 11. The apparatus of claim 10, wherein said reference electrode is modified to inhibit cell growth and/or adhesion thereon.

12. The apparatus of claim 11, wherein the modification comprises coating said reference electrode with a substance that inhibit cell growth and/or adhesion.

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13. The apparatus of claim 11, wherein the modification comprises altering the surface topography of said reference electrode.

14. The apparatus of claim 11, wherein the modification comprises depositing islands
20 of insulating material on said electrode, wherein the separation between adjacent islands is less than half the diameter of a cell.

15. The apparatus of claim 11, wherein the modification comprises depositing islands of insulating material on said reference electrode, wherein the island has a height from the surface of said reference electrode of about 1/4 to 3/4 the diameter of a cell and a diameter of less than about 1/4 the diameter of the cell.

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16. The apparatus of claim 10, wherein said reference electrode is sandwiched between said insulating layer and said substrate.

17. The apparatus of claim 1, wherein said electrodes are sandwiched between said
10 insulating layer and said substrate.

18. The apparatus of claim 1, wherein said insulating layer is constructed of silicon, plastics, pure silica or other glasses.

15 19. The apparatus of claim 1, wherein said substrate is constructed of silicon, plastics, pure silica and other glasses.

20. The apparatus of claim 1, wherein each orifice is fluidly connected to at least one microfluidic channel.

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21. The apparatus of claim 20, wherein the at least one microfluidic channel is located between the insulating layer and the substrate.

22. The apparatus of claim 1, wherein the substrate defines the bottom of a well of a multi-well plate.

23. A method for performing multiplexed patch clamping and fluorescence assays

5 comprising the steps of:

providing the apparatus of claim 1;

attaching a cell on each of said plurality of orifices to form an electrically resistive seal of about $1\text{M}\Omega$ to $1\text{G}\Omega$ around the orifice; and

performing patch clamping and fluorescence assays on the cell.

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24. The method of claim 23, wherein the attaching step is accomplished by growing the cell on the orifice or allowing the cell to migrate over the orifice under cellular motility.

15 25. The method of claim 23, wherein the performing step comprises

exposing the cell to a test compound; and

measuring a current across the cell membrane and/or a fluorescent signal indicating cellular activity in response to the test compound.

20 26. The method of claim, 23 wherein each of said plurality of orifices has a diameter of about $0.5\text{-}5\text{ }\mu\text{m}$.

27. The method of claim 23, wherein said electrodes is a ITO electrode.

28. The method of claim 23, wherein each electrode is electrically isolated from the other electrodes.

5 29. The method of claim 23, wherein a part of each of said electrode is electrically connected to an orifice.

30. The method of claim 23, wherein each orifice is electrically connected to two electrodes.

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31. The method of claim 30, wherein one of the two electrodes is a sensing electrode and the other electrode is used to deliver an electrical signal to the orifice.

15 32. The method of claim 23, wherein an area adjacent to each orifice is coated with a substance to promote cell growth and/or adhesion.

33. The method of claim 32, wherein the substance to promote cell growth and/or adhesion is silica (SiO_2), polylysine, and/or collagen.

20 34. The method of claim 23, further containing a reference electrode.

35. The method of claim 34, wherein said reference electrode is modified to inhibit cell growth and/or adhesion thereon.

36. The method of claim 35, wherein the modification comprises coating said reference electrode with a substance that inhibit cell growth and/or adhesion.

5 37. The method of claim 35, wherein the modification comprises altering the surface topography of said reference electrode.

38. The method of claim 35, wherein the modification comprises depositing islands of insulating material on said electrode, wherein the separation between adjacent islands is
10 less than half the diameter of a cell.

39. The method of claim 35, wherein the modification comprises depositing islands of insulating material on said reference electrode, wherein the island has a height from the surface of said reference electrode of about 1/4 to 3/4 the diameter of a cell and a
15 diameter of less than about 1/4 the diameter of the cell.

40. The method of claim 34, wherein said reference electrode is sandwiched between said insulating layer and said substrate.

20 41. The method of claim 23, wherein said electrodes are sandwiched between said insulating layer and said substrate.

42. The method of claim 23, wherein said insulating layer is constructed of silicon, plastics, pure silica or other glasses.

43. The method of claim 23, wherein said substrate is constructed of silicon, plastics,
5 pure silica and other glasses.

44. The method of claim 23, wherein each orifice is fluidly connected to at least one microfluidic channel.

10 45. The method of claim 44, wherein the at least one microfluidic channel is located between the insulating layer and the substrate.

46. The method of claim 23, wherein the substrate defines the bottom of a well of a multi-well plate.

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47. The method of claim 23, further comprising the step of centrifuging the apparatus of claim 1 to press the cell against the orifice to ensure an electrically insulative seal of about $1\text{M}\Omega$ to $1\text{G}\Omega$.